Table 1 Frequencies of HLA Class I Alleles That are Known to Serve as HIV CTL Restriction Elements in Four Populations

	Frequencies*					
HLA	African	USA	North American			
Alleles	Americans	Caucasians	Indians	Thais		
A2	16.7	28.3	25.5	25.5		
A3	8.9	12.2	2.9	1.5		
AII	2.3	5.5	1.0	32.5		
A24	4.7	9.6	19.6	14.6		
A28	10.9	4.5	6.9	0.3		
A30	9.5	2.6	2.0	1.1		
A31	1.7	2.0	27.5	1.7		
A32	1.0	5.1	2.0	0.2		
A33	8.1	1.0	1.0	13.6		
В7	8.3	10.0	3.9	2.7		
B8	3.2	10.0	5.6	0.2		
B12 (44)	6.2	10.4	3.9	5.4		
B13	0.9	3.0	1.0	9.3		
B14	3.0	4.1	2.9	0.4		
B17	10.9	4.9	1.0	8.1		
B18	3.3	4.9	1.0	2.5		
B27	1.6	4.1	2.9	6.0		
B35	7.7	8.5	18.6	2.5		
B37	0.9	2.2	0.0	1.4		
B52	1.1	1.2	2.9	3.1		
B53	12.8	0.8	0.0	0.0		
B <i>5</i> 7	4.2	3.9	1.0	5.2		
360	1.3	4.5	2.9	8.3		
B62	1.4	5.5	4.9	5.0		
Cw3	9.6	12.6	22.4	15		
Cw4	21.0	9.8	15.4	6		

\*Frequencies for HLA-A and HLA-B alleles are taken from HLA 1991 [21], HLA-C for African Americans and USA Caucasians are taken from Histocompatibility Testing 1984 [19], HLA-C for North American Indians from Williams and McAuley, 1992 [22], and HLA-C for Thais from the Proceedings of the Second Asia and Oceania Histocompatibility Workshop Conference [23].

Table 2 Proportion of each of the four populations that would be predicted to present peptides to the immune system

Population	HLA Restriction Elements Chosen	HIV Protein	Epitope Location	Epitope
a) African Americans	A2, A3, A11, B35	nef	73-82	
a) African Americans	A28, B14	ner gp41	73-82 583-592	QVPLRPHTYK
	A30. B8	gp41	844-863	VERYLKDQQL RRIROGLERALL
	B17. B37	nef	117-128	-
	Cw4	gp120	576-383	TQGYFPQWQUYT (S) FNCGGEFF
(Proportion of African )	= '			
b) USA Caucasians	A2, A3, A11, B35	nef	73-82	QVPLRPMTYK
	A30, B8	gp4 l	844-863	RRIRQGLERALL
	B7	gp120	302-312*	RPNNNTRKSI
		nef	126-138*	NYTEGEGVRYPLT
	B12	p24	169-184	IPMFSALSEGATPQDL
Proportion of USA Cau	scasians expected to pr	esent these	4 epitopes is 9	0.2%)
) North American	A2, A3, A11, B35	nef	73-82	OVPLRPMTYK
Indians	A24	gp4 [	584-591*	YLXDQQL
		nef	120-144*	YFPDWQNYTPGPGIRYPLTFGWCYK
	A31	gp4 [	770-780	RLRDLLLIVTR
Proportion of North An	nerican Indians expect	ed to presen	t these 3 epitoj	oes is 96.4%)
i) Thais	A2, A3, A11, B35	nef	73-82	OVLRPMTYK
	A24	gp41	584-591*	YLXDCOL
		nef	120-144*	YFPDWQNYTPGPGIRYPLTFCGWCY
Proportion of Thais exp	pected to present these	2 epitopes i	93.6%)	
African Americans	A2, A3, A11, B35	nef	73-82	OVPLRPMTYK
USA Caucasians North American	A28, B14	gp41	583-592	VERYLKDÇQL
ndians	A30, B8	gp41	844-863	RRIRGGLERALL
Thais	B17, B37	nef	117-128	TOGYFPOWONYT
	Cw4	gp120	376-383	(S) FNCGGEFF
	B7	gp120	302-312*	RPNNNTRKSI
		nef	126-138*	NYTPGPGVRYPLT
	B12	p24	169-184	IPMFSALSEGATPQDL
	A31	gp4 I	770-780	RLRDLLLIVTR
	A24	gp4 I	584-591*	AFKDCOF
		nef	120-144*	YFPDWQNYTPGPGIRYPLTFCGWCY

(Proportions of African Americans, USA Caucasians, North American Indians, and Thais expected to present these 9 epitopes are 95.4%, 97.5%, 99.4%, and 97.2%, respectively)

<sup>&</sup>quot;The criteria upon which choices among peptides should be made are not yet known. It may be important to choose peptides that have been reported to be immunogenic in non-progressors to AIDS or that have been reported to induce immunodominant anti-HIV T-cell responses.



### TABLE 3

### Th-CTL Pepude Proscrype Vaccine Immunogens for Testing in Either Mice, Rhems Macaque or Human

Vaccine	Name of Persudes	Species us which o		Restricting elements for .
l.	Mouse HIV-1 Th-CTL epitopes	be studied	Amuno acid sequence Th - CTI.	CTL epitope
	A-TWA-CTL	Mouse	HAGP LAPGCHREPRG-KQIIMMQEVGKANYA	H-3-
	B-Th/8-CTL	House	KEKVYLAMVPAHKGIG-HYAPPIGGQI	H-5 K-
	C-Th/C-CTL	Youse	QLLFIHFRIGCRHSR-DRVIEWVQGAYRAIR	H-Mann (Dr)
	D-TIVD-CTL	Mouse	EQMHEDITSLWDQSL-RIHIGPGRAFYTTKN	H-2 D*
3.	Macaque SIV/HIV-1 Th-CTI epitopes		ть - ст.	
	Thi/CTL/SIV Gag	Macaque	ELYKYKVVKIEPLGVAPTKA-CTPYDINGM	Mamu-A*91
	Th2/CTL/SIV Pol	Macaque	VST/CCTHGIRPVVSTQLLL-STPPL/RL	Mamu-A*01
	Th3/CTL/HIV-1 Env	Macaque	STSIRGKVQKEYAFFYKLDI-YAPPISGQI	<b>Мали-</b> А*01
5.	Macaque SIV/HIV-1 Th-CTL p11c epitopes variants		Th - CTL	
	Thi/CTL/SIV Gug	Hacaque	ELYKYKVVKIEPLGVAPTKA-CTPYDINGM	Mamu-A*01
	Thirt CTL/ SIV Gagpi loi-Y	Macaque	VSTVQCTHGIRPVVSTQLLL-CTPYDYNQML	Mamu-A*01
	Th3/CTL/ SIV Gag/pi lot-A	Macaque	STSIRGKVCKEYAFFYKLDI-CTPYDANCHL	Mamu-A*01
	Th-VCTL/ SIV Gaypila/ID	Macaque	EYAFFYKLDIIFIDMDTTSY-CTPYCONQML	Mamu-A*01
	This/CTL/ SIV Gagpille/LK	Macaque	REGFGMMKTIIFKQSSGGDPE-CTPYDKNQML	Mamu-4*01
6.	Human HIV-1 Th-CTL overlapping epitopes		Th - CTL	
	A-Th/A-CTL	Human	KÇIIZMWÇEVGKAMYA-KAFSPEVIPMF	HLA B57.B58
	B-Th/B-CTL	Human	YERMITLGLMET/RHYS-MPPIPVGETYRRMI- TLGLMET/RHYSPTSI	HLA B35.B8.B27.A33.Bw62.B52
	C-Th/C-CTL	Human	DRVIEVVQGAYRAIR-VGFPVRPQVPLRPMTYK	HLA A1.87.88.835.A11.A2.A3.A31
	D-Th/D-CTL	Human	ASLWMWFNITHWLWY-WYHTQGF79DWQNYTP	HLA B7.B57.A1.B8.B18.B35
8.	Human HIV-1 Th-dominant			
	subdominant CTL epitopes A-Th/E-CTL	Human	Th CTL KO NAMOSVGKANYA-SLOVEVATA	HLA A2
	B-Th/F-CTL	Human	YKRWIIIGLNKIVRMYS-KIRLRPGGK	HLA A3
	C-TWG-CTL	Human	DRVIEWQGAYRAIR-KRWIILGLWK	HLA B27
	D-TMH-CTL		ASL/MWFNITNWLWY-GGKKKYKL	
	D-TMH-CTL E-TMI-CTL	Human	MREPROSKIAGTTST-ERYLKDOOL	HLA BI4
10.			TREEMSKEASTEST-SKYCKDQC	HLA BIA
10.	Human HIV-1 Th-CTL p17 epitope (A2 Variants)		Th - CTL	
	B-Th/E-CTL	Human	YKRWIILGLNKIVRHYS-SLYNTVATL	HLA A2
	C-TMJ-CTL	Human	DRVIEWQGAYRAIR-SLFNTVATL	HLA A2
	A-TWK-CTL	Human	QIINMWQEVGKAMYA-SLYNAVATL	HLA A2
	D-TML-CTL	Human	ASLANWENITHWLWY-SLYNT/AVL	HLA A2
	E-Th/M-CTL	Human	MREPROSKIAGTTST-SLFMLLAVL	HLA A2

Vaccine	Amino acid	recusence			Restricting elements for
11. Human HIV-1 Th-CTL overlapping epitopes	Th		CTL		
A*-Th/J-CTL	KQIINMWQVVG	KAMYA-G	OMVHQAIS	PRTLNAWVKVV	A2, A202,A5, B7, B14, B57, B5701, B5801, B02, Cw3
A*-Th/K-CTL	KQIINMWQVVG	KAMYA-A	PODLNTM	LNTVGGHQAAMQMLKETINEEAAEW	A2.A25, A26, B7, B12, B14, B1402, B27, B39, B52, B53, B57, B58, B8101, Cw8, Cw0102

A\*-TIML-CTL KQIINGNQVVGKAMYA-GGKEPFRDYVDRFYXTLRAEQASGEVXDRØHT 8.2.A102.A5.A13.424.A28.A26.A13.87.

A\*-TIMM-CTL KQIINGNQVVGKAMYA-KKRLRFGGKKKYKLKHIVWGSEELRSLYNTVATLYCVHQRI ALALAA.A1.A103.A11.A23.A24.A0201.
A2-TIMM-CTL KQIINGNQVVGKAMYA-KKRLRFGGKKKYKLKHIVWGSEELRSLYNTVATLYCVHQRI ALALAA.A1.A103.A11.A23.A24.A0201.
A2-402.B3.B27.B42.B62.Bw62.Cw4



# Table 4

Linear Array of Th-CTL Epitopes To Be Expressed in Modified Vaccinia Ankara
MVA-1) HIV-1 mouse Th-CTL epitopes in
A-TTV 024' (H-2 b) A-CTTV gp (20 (H-2 abf ) B-TTVRT (H2 alk ) B-CTTV gp (20 (H-2K d)
HAGPIAPGQMREPRGKQIINMWQEVGKAMYAKEKVYLAWVPAHKGIGMYAPPIGGQI-
- C-Thyror(H-2 d) - C-CTL/gp41(H-2 dpag (D d-D-Th/gp120(H-2 d) - D-CTL/gp420/H-2D d)QLLFIHFRIGCRHSRDRVIEVVQGAYRAIREQNHEDIISLMDQSLRIHIGPGRAFYTTXN
MVA-2) p55/gag + the same HIV-1 mouse Th-CTL epitopes in MVA-1
MVA-3) HIV-1/SIV Th-CTL epitopes in
Th/gp120/DR8*w201 CTUSIV Gag (Mamu-4*01) Th2/gp120/DR8*5406 CTUSIV Pol (Mamu-A*01) ELYKYKVVK1EPLGVAPTKA
Thingpt20 CTLHW-1 Eav (Manus-A*91)STSIRGKYQKEYAFFYKLD:
MVA-4) p55/gag + the same HIV-1/SIV Th-CTL epitopes in MVA-3
MVA-5) SIV Th-CTL p11c epitope variants in
Thi/DR8*w201 CTLSIV Gag (Mamu:A*01) Thi/DR81*\$406 CTLGaypo:101-Y  BLYKVKVV/KEEPLGVAPTKA - CTPYDINOML - VST/OCTHGIRPV/STOLL: - CTPYDYNGML-
Thi/Pi4 CTL Gagotlott-A Thi/Pi5 CTL Gagotlott-A
-STSIRGKVQKEYAFFVKLDICTPYDANQMLSYAFFYKLDIIFIDNDTTSYCTPYDENQML-
ThS/P33 CTL/Gaypilat-K -REQFGNNKTIFKQSSGGDEECTPYDKNQML
MVA-6) HIV-1 human Th-CTL overlapping epitopes in
A-Th/gpt20/422-437 A-CTL624/30-40 B-Th/GTH///30-146 B-CTLP24/21-150 KQIINMWQEVGKAMYAXAFSPEVIPMFYKRWIIJGLNKIVRMYSNPPIPVGSIYKRWIIJGLNKIVRMYSPTSI-
C-Th/gp41/317-331 C-CTLNet/64-80 D-Th/gp41/157-171 D-CTLNet/111-12TDRVIEWVQGAYRAIRVGFFVRPQVPLRPMTYKASLANWENITAWLWYWYHTQGFFFDMCWYTF
Restricting elements for CTL epitopes:
A-CTL epitope::«HLA B57/B5%: B-CTL epitope::HLA B35/B8/B27/A33/Bw62/B52; C-CTL epitope::HLA A1//B7/B8/B35/A11/A2/A33/A31); D-CTL epitope::HLA B7/B57/A1/B8/B13/B35.
MVA-7) p55 gag +the same HIV-1 human Th-CTL overlapping epitopes in MVA-6
MVA-8) HIV-1 Thdominant/subdominant CTL epitopes in
A-THUCH422-437 E-CTRUBITAT-85(AZ) B-THUGTHIMISO-146 F-CTLUBTAS-56(A3) C-THUGHIMIST-331 KOLINDWCEVGKAMYASUVNTYATLYARWILLGINKUVRYSKIRLRPGGKDRVIEWZGAYRAIR-
-G-CTLp24/131-(40/827) -D-Tb/gp41/157-(71 H-CTLp17/24-31/88) -E-Tb/g246-110 -I-CTLg24/74-82(814)
KRWIIIGLNKASIMNWFNITNWIWYGGKKXYKLMREPRGSKIAGTTSTERYLKDQQL-
MVA-9) p55/gag + the same HIV-1 Th-dominant/subdominant CTL epitopes in MVA-8
MVA-10) HIV-1 Th-CTL A2 p17 epitope (A2 Variants) in
B-Th/GTH//130-146 E-CTL/p17/77-85(A2) C-Th/gp4//317-331  -L-CTL/p17/Camsensus A   A-Th/C4/422-437    YKRW2 LGLMKI/RMYS
K-CTL/P17/RF D-Tb/ep41/157-171 L-CTL/P17/Consensus F E-Tb/p2496-110 M-CTL/P17/V1525
SLYNAVATLASLWNWFNITNWLWYSLYNTVAVL



	-	
Peptide	gp120 C4 Region	gp120 V3 Region
C4-V3MIN	KQIINMWQEVGKAMYATR	PNYNKRKRIHIGPGRAFYTTK
C4-V3RF	KQIINMWQEVGKAMYATR	PNNNTRKSITKGPGRVIYATG
C4-V3EV91	KQIINMWQEVGKAMYATR	PGNNTRKSIPIGPGRAFIATS
C4-V3CanOA	KQIINMWQEVGKAMYATR	PHNNTRKSIHMGPGKAFYTTG
C4E9G-V3RF	KQIINMWQGVGKAMYATR	PNNNTRKSITKGPGRVIYATG
C4E9V-V3RF	KQIINMWQVVGKAMYATR	PNNNTRKSITKGPGRVIYATG
C4K12E-V3RF	KQIINMWQEVGEAMYATR	PNNNTRKSITKGPGRVIYATG





## TABLE 6

#### Th-CTL Peptide Prototype Vaccine Immunogens derived from HIV-1 gag

Vaccine  number Name of Pentides  Human HIV-I Th-CTL  overlapping epitopes		Amino acut semence Th - CTL	Restricting elements for CTL entiting
6	A-Th/A-CTL	KQIINMWQEVGKAMYA-KAPSPEVIPMP	B57,B58
6	B-Th/B-CTL	YKRWIILGLNKIVRMYS-NPPIPVGEIYKRWIILGLNKIVRMYSPTSI	B35,B8,B27,A33,Bw62,B52
11	A*-Th/J-CTL	KQIINMMQVVGKAMYA-GQMVHQAISPRTLNAWVKVV	A2, A202,A5, B7, B14, B57, B5701, B5801, B02, Cw3
11	A*-Th/K-CTL	KQIINMWQVVGKAMYA-ATPQDLATMLNTVGGHQAAMQMLKETINEEAAEW	A2,A25, A26, B7, B12, B14, B1402, B27, B39, B52, B53, B57, B58, B8101, Cw8, Cw0102
11	A*-Th/L-CTL	KQIINNWQVVGKAMYA-GPKEPFRDYVDRFYKTLRAEQASQEVKNWMT	A2,A202,A5,A24,A2402,A25,A26,A33, B7, B8,B12, B14 B35,B39, B44, B52, B53Bw62, B27, B2705, B57, B5701;
11	A*-Th/M-CTL	KQIINMWQVVGKAMYA- KIRLRPGGKKKYKLKHIVWGSEELRSLYNTVATLYCVHQRI	B70. B71.Bw62. Cw3. Cw8. Cw0401 A1,A2,A3, A3.1,A03. A11, A23, A24, A0201, A2402, B8, B27, B42, B62, Bw62, Cw4

### A\*-Th=C4E9V

### Summary of restracting elements for CTL eptopes in Vaccines A, B, J, K, L and M

- A: A1, A2 (02), (01), A3, A3.1, A5, A11, A23, A24 (02), A25, A26 and A33.
- B: B7, B8, B12, B14 (02), B27 (05), B35, B39, B42, B44, B52, B53, B57 (01), B58 (01) B62 (w62), B70 and B71.
- C: Cw3, Cw4, Cw0401 and Cw8.

HIV TWCTL vaccine ABJKLM